INTRODUCTION

Clinical heart transplantation was made possible by the considerable experimental work carried out earlier this century, which embraced mainly the technical, physiological and immunological aspects of the procedure. This chapter endeavour to review briefly the evolution and results of experimental surgical techniques utilized by cardiac transplant research workers; a comprehensive review appears elsewhere.

Experimental work on cardiac transplantation evolved through several overlapping phases. In the earliest experiments animals were given a second, often parasitic, heart which enabled certain physiological, pharmacological and pathological studies to be made. Initially the neck was chosen as the locus, though the abdomen and inguinal regions were occasionally used. The subsequent evolution of surgical techniques permitted the insertion of the donor heart into the chest as an auxiliary pump in circuit with the recipient organ. With the advent of hypothermia and the pump-oxygenator, total excision and replacement of the recipient heart became more feasible. Finally, after technical and physiological problems had been studied and minimized, efforts were made to combat the immune response with immunosuppressive agents.

TRANSPLANTATION OF AN ACCESSORY HEART

The first reported attempts at experimental heart transplantation were by Carrel (Figure 1) and Guthrie in 1905. The principal technique they used is inadequately described as 'anastomosing the cut ends of the jugular vein and the carotid artery to the aorta, the pulmonary artery, one of the vena cava and a pulmonary vein. Although contractions of the donor atria appeared immediately, effective contractions of the ventricles did not begin for approximately 1 hour. The experiment was interrupted after a further 2 hours when coagulation occurred in the cavities of the heart.

The crucial factor of donor coronary perfusion (vivipерfusion) was simplified in 1933 when Mann and his colleagues developed a technique of cervical transplantation (Figure 2). Numerous investigators have subsequently used modifications of the Mann technique to study problems of heart transplantation and the response of the denervated heart to pharmacological agents and physiological stresses. One such modification remains a standard model in many laboratories, including our own, for experimental animal studies on acute rejection and immunosuppression (Figure 3).
Figure 2. Technique of experimental heterotopic heart transplantation in the neck (Mann et al., 1933). I.J.V. = internal jugular vein; R.C.C.A. = right common carotid artery.

Figure 3. Modification of the Mann experimental cervical heterotopic heart transplantation technique as used in our own laboratory.

From their results, Mann and his co-investigators concluded that a functioning cardiac allograft was no less 'resistant' than a renal allograft, the graft failing to survive due to the same 'biologic factor' which also prevented survival of other homografts and homotransplanted tissues and organs. Such a transplanted heart, however, proved a valuable test object for the investigation of various physiological problems. For example, the effect of the intravenous administration of thyroxine to the host animal was investigated; the denervated donor heart was demonstrated to be more sensitive to the accelerating influence of the drug since central nervous system influence was inhibitory.

In more recent years, techniques for transplanting the auxiliary donor heart into the abdomen of the recipient have been described, principally for the study of the immune response and its modification by therapeutic agents (Figure 4); using microsurgical techniques it remains an important experimental model in rats.

Figure 4. Technique of experimental heterotopic heart transplantation in the abdomen (Abbott et al., 1964).

THE TRANSPLANTED HEART AS AN AUXILIARY INTRATHORACIC PUMP

In 1946, Demikhov (Chapter 66, Figure 1) began extensive studies on transplantation of the heart into the thorax. These involved the addition of a second heart (occasionally with an attached lobe of a lung) as an auxiliary pump, as well as orthotopic transplantation of the heart with and without both lungs. The ambitious nature of Demikhov's attempts can be appreciated best when it is remembered that supportive techniques, such as hypothermia and cardiopulmonary bypass, had not yet been developed.

In all, Demikhov described 24 variants of his technique to place an additional heart within the thorax, performing 250 operations on dogs utilizing most of the major vessels within the chest cavity. Few animals survived more than a few days, most of the early deaths being associated with technical problems. The best results with regard to functional activity of the transplanted heart and preservation of its structure were obtained after operations using the technique illustrated in Figure 5. Physiologically the transplanted heart was distinguished by the comparative constancy of its rhythm and by its greater resistance to the action of toxic doses of various cardiac glycosides. The physiological and pharmacological responses of the denervated, transplanted heart are discussed more fully in Chapter 27.